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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,239	02/27/2002	Simon Ward	674569-2001	1714

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EXAMINER	
ROYDS, LESLIE A	

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1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/085,239	WARD ET AL.	
	Examiner	Art Unit	
	LESLIE A. ROYDS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-42,44-46 and 48-50* is/are rejected.

7)☒ Claim(s) *43,47,51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 40-51 are presented for examination.

Applicant's Amendment filed April 20, 2009 has been received and entered into the present application.

Claims 40-51 remain pending and under examination. Claims 40-50 are amended.

Applicant's arguments, filed April 20, 2009, have been fully considered. Rejections and objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set of rejections and objections presently being applied to the instant application.

Error Noted in Claim Listing of April 20, 2009

Applicant is notified that the claim listing of April 20, 2009 fails to properly set forth the text of the pending claim relative to the text of the immediately prior version of the claims. Specifically, it is noted that Applicant has newly added the phrase "consisting of" in instant claim 41 following the phrase "from the group" and prior to "psoriasis" in line 3 of claim 41. However, such a newly added limitation has not been properly underlined to indicate its addition pursuant to the requirements of 37 C.F.R. 1.121(c).

Applicant is urged to comply with the provisions of 37 C.F.R. 1.121(c), which requires strikethrough or bracketing to show what has been removed from the claim and underlining to show what has been added to the claim as compared to the **immediately prior version of the claims**. Applicant is herein respectfully requested to comply with the requirements for proper claim amending as set forth in 37 C.F.R. 1.121(c) of the same in the event that Applicant should choose to submit any subsequent claim listings to the Office.

Objection to the Claims (New Grounds of Objection)

Claims 43, 47 and 51 are objected to for depending upon a rejected base claim, but would otherwise be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the therapeutic objective of instant claim 48 is the treatment of a disease selected from psoriasis, acne vulgaris, solar keratosis, squamous carcinoma *in situ*, cancers and pre-malignant conditions, ichthyoses, hyperkeratosis and disorders of keratinization (i.e., Darier's disease as claimed in dependent claim 51), but the patient to be treated via the instantly claimed method is a patient in need of treatment for psoriasis. As a result, the connection between the purpose of the instantly claimed method (i.e., for the treatment of psoriasis, acne vulgaris, solar keratosis, squamous carcinoma *in situ*, cancers and pre-malignant conditions, ichthyoses, hyperkeratosis and disorders of keratinization) and the actual patient to be treated is not clearly set forth in the instant claims, since the claims appear to circumscribe the treatment of various hyperproliferative skin disorders, but are only practiced in a subject that suffers from only one of the claimed hyperproliferative skin disorders. Accordingly, one of ordinary skill in the art at the time of the invention would not have been reasonably apprised of the metes and bounds of the subject matter for which Applicant is presently seeking protection.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 40-42, 44-46 and 48-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burchardt et al. (WO 97/15298; 1997), already of record, for the reasons of record set forth at p.4-8 of the previous Office Action dated October 21, 2008, of which said reasons are herein incorporated by reference.

Newly amended claims 40-42, 44-46 and 48-50 remain properly included in the present rejection because Burchardt et al. teaches the treatment of acute and chronic inflammatory disorders, such as psoriasis (p.6, l.1-11), using a glucocorticosteroid, of which carbenoxolone sodium is specifically named, and an LTD4 receptor antagonist (p.1, p.4-6- and p.2, l.3-7). Burchardt et al. expressly discloses that the combination can be used topically as an ointment or cream for application to the skin (p.6, l.18-20).

Applicant's amended claims are directed (1) a method of treating a hyperproliferative disease of the skin subject to treatment by inhibition of the retinoic acid biosynthetic pathway, wherein the disease is, *inter alia*, psoriasis, consisting of administering to a patient in need of treatment for a hyperproliferative disease of the skin a pharmaceutical composition, wherein the pharmaceutical composition consists of a single inhibitor of the retinoic acid biosynthetic pathway which is carbenoxolone and one or more pharmaceutically acceptable carriers, diluents or excipients (claims 40-42 and 48-50) or (2) a method of treating a hyperproliferative disease of the skin subject to treatment by inhibition of the retinoic acid biosynthetic pathway, wherein the disease is, *inter alia*, psoriasis, by topically administering to skin that is to be treated of a patient in need of treatment for a hyperproliferative disease of the skin, a pharmaceutical composition consisting of a single inhibitor of the retinoic acid biosynthetic pathway, which is carbenoxolone and one or more pharmaceutically acceptable carriers, diluents or excipients, wherein the instant specification states that, "Each carrier should be 'acceptable' in the sense of being compatible with the other ingredients in the formulation and not injurious to the patient. The carrier should be biologically acceptable without eliciting an adverse reaction (e.g., immune response) when administered to the host." (p.71, l.15-18) In light of such properties, the LTD4 receptor antagonist of Burchardt et al. meets Applicant's limitation directed to a "pharmaceutically acceptable carrier" because (1) it is clearly compatible with the other agents in the formulation, (2) is also clearly not injurious to the subject to be treated, since it is formulated specifically for pharmaceutical use, and (3) does not produce an adverse reaction, such as an adverse immune reaction, since it is taught by Burchardt et al. to treat acute and chronic inflammatory processes via LTD4 antagonism, which produces a desirable antagonizing effect on leukotriene production in order to treat inflammation (i.e., does not produce an *adverse immune reaction*). Accordingly, Burchardt et al. provides for the (topical) administration of a composition consisting of carbenoxolone (i.e., the inhibitor of the retinoic acid biosynthetic pathway as instantly claimed) with an LTD4 receptor antagonist (considered, in this case, to be equivalent to the

"carrier" of Applicant's claims) to a subject (or the affected skin of said subject) in need of treatment of psoriasis, which meets Applicant's limitations of claims 40-42, 44-46 and 48-50.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the terms "carrier", "diluent" and "excipient" are well-known in the art and, therefore, it is not necessary to define them in the specification and relies on the *Hybritech Inc.* case in view of his position. Applicant states that carriers, diluents, and excipients are defined in Remington's and alleges that it would be clear to the skilled person that carriers, diluents and excipients should not have any biological activity and are included only to enable the active agent to be administered to the patient. Applicant further alleges that the LTD4 antagonist of Burchardt et al. is biologically active and, thus, cannot be defined as being a carrier, diluent or excipient. Still further, Applicant asserts that the specification at p.71 states that the carrier should not elicit an adverse reaction (e.g., immune response) when administered to the host and alleges that the function of the LTD4 antagonist "by its nature and design" elicits an immune response and is, therefore, excluded from fitting the definition of a "carrier" in accordance with the instant invention. Applicant alleges that the combined formulation of carbenoxolone sodium and an LTD4 antagonist as taught by Burchardt et al. "could even elicit an adverse reaction in a patient in need of treatment of a hyperproliferative disorder of the skin" (Remarks, p.3) and submits that there is no motivation to use only carbenoxolone as the sole active agent to treat the recited disorders.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, while it is agreed that a patent specification need not teach, and preferably omits, what is well known in the art, such an argument is unpersuasive in establishing that "pharmaceutically acceptable carriers, diluents or excipients" are so well known in the art so as to implicitly exclude the LTD4 receptor antagonist of Burchardt et al. Applicant has failed to specifically point out that how the state of the art

was sufficiently well-developed that one of skill in the art would have reasonably understood that such a compound would not have been considered a pharmaceutically acceptable carrier, diluent or excipient. Applicant diffusely references Remington's as allegedly providing support for his allegation that the LTD4 antagonist of Burchardt et al. would not be considered a carrier, diluent or excipient, but fails to provide any copy of the specific disclosure from this reference upon which he relies to document his position. Moreover, Applicant then attempts to define "carrier", "diluent" or "excipient" at p.3 of the Remarks such that "one of skill would recognize that: a 'carrier' relates to an inactive compound which is combined with the active agent in a drug formulation, and is provided to facilitate administration of the formulation to a patient; a 'diluent' relates to an inert ingredient added to a pharmaceutical in addition to the active drug; and an 'excipient' relates to an inactive substance used as a carrier for the active ingredients of a medication". However, these alleged definitions (1) do not appear in the instant specification and (2) Applicant provides no documentation to support these supposed and allegedly limiting definitions of "carrier", "diluent" or "excipient" as being well-known and accepted in the art. Statements of this nature are unsupported allegations and are clearly unpersuasive in accordance with the guidance provided at MPEP §2145, which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997)".

Secondly, the allegation that the carrier(s), diluent(s) and/or excipient(s) should not have any biological activity such that the LTD4 antagonist, which has biological activity as an antagonist of leukotrienes, is excluded from the instant claims is (1) Counsel's own opinion and is unsupported by any documentation to this effect, which is unpersuasive pursuant to MPEP §2145 (see *supra*) and (2) is not a point well taken. For example, water is frequently used as a pharmaceutical carrier and is also essential for various metabolic processes and is required for adequate bodily hydration. Such effects clearly constitute "biological activity" and, therefore, the idea that all carrier(s), diluent(s) and/or excipient(s)

must not have any "biological activity" appears to be inconsistent with the art. Thus, these allegations that a carrier, diluent or excipient must be free of biological activity in order to be considered a pharmaceutically acceptable carrier, diluent or excipient are clearly unimpressive in establishing that the LTD4 receptor antagonist of Burchardt et al. does not meet Applicant's requirement for one or more pharmaceutically acceptable carriers, diluents or excipients.

Thirdly, Applicant attempts to rely upon p.71 of the instant specification to support his allegation that the function of the LTD4 antagonist is to elicit an immune response, which is allegedly excluded from fitting the definition of a carrier in accordance with the instant invention. This is, and will remain, unpersuasive. Applicant clearly states at p.71 of the instant specification that, "Each carrier should be 'acceptable' in the sense of being compatible with the other ingredients in the formulation and not injurious to the patient. The carrier should be biologically acceptable without eliciting an adverse reaction (e.g., immune response) when administered to the host." (p.71, l.15-18) In light of such properties, the LTD4 receptor antagonist of Burchardt et al. meets Applicant's limitation directed to a "pharmaceutically acceptable carrier" because (1) it is clearly compatible with the other agents in the formulation, (2) is also clearly not injurious to the subject to be treated, since it is formulated specifically for pharmaceutical use, and (3) does not produce an *adverse* reaction, such as an adverse immune reaction, since it is taught by Burchardt et al. to treat acute and chronic inflammatory processes via LTD4 antagonism, which produces a desirable antagonizing effect on leukotriene production in order to treat inflammation (i.e., does not produce an *adverse immune reaction*).

Though Applicant alleges that the LTD4 antagonist "elicits an immune response", once again, this is an allegation without any factual support. Applicant has failed to provide any evidence that (1) the LTD4 antagonist elicits an immune response or (2) even if, *arguendo*, the LTD4 antagonist did elicit an immune response (which the Examiner does not concede), there is no evidence of record to show that this is an "adverse" immune response. Note that p.71 states it should not elicit *an adverse reaction (e.g.,*

immune response), which is understood to mean that it should not elicit an *adverse immune response*, which for the reasons described above, it does not. Accordingly, Applicant again has failed to demonstrate that the LTD4 antagonist of Burchardt et al. is excluded from fitting the definition of a "carrier" in accordance with the instant invention.

Fourthly, Applicant alleges that the combined formulation of carbenoxolone sodium and an LTD4 antagonist as taught by Burchardt et al. "could even elicit an adverse reaction in a patient in need of treatment of a hyperproliferative disorder of the skin" (Remarks, p.3). This is unpersuasive. Applicant provides absolutely no basis in fact, documentation or evidence to support this allegation and, as a result, this statement is clearly an allegation without merit. Moreover, Applicant is again reminded that Burchardt et al. very clearly teaches the treatment of acute and chronic inflammatory disorders, such as psoriasis (p.6, l.1-11), using a glucocorticosteroid, of which carbenoxolone sodium is specifically named, and an LTD4 receptor antagonist (p.1, p.4-6- and p.2, l.3-7), wherein Burchardt et al. also discloses that the combination can be used topically as an ointment or cream for application to the skin (p.6, l.18-20). In view of such teachings that the disclosed combination can be used for the treatment of, *inter alia*, psoriasis, there is no basis in Burchardt et al. to allege that there would be adverse reaction in a patient in need of treatment of the hyperproliferative disorder psoriasis using the disclosed combination since Burchardt et al. explicitly teaches that this combination can be used for the treatment of the same. The disclosure of the combination's ability to treat the disease does not then support Applicant's assertion that the same combination would have a negative or adverse effect in a patient with the same disease. Such remarks are, therefore, clearly unpersuasive.

Fifthly, and lastly, Applicant alleges that there is no motivation to use carbenoxolone as the sole active agent to treat the recited disorders. This is also unpersuasive because the instant claims are neither specifically limited to carbenoxolone alone nor are limited to carbenoxolone as the "sole active agent" in the claimed composition. As a result, the argument that the references fail to show these features of

Applicant's invention is unimpressive because these features upon which Applicant relies are not recited in the rejected claim(s). The instant claims provide for the administration of a pharmaceutical composition consisting of carbenoxolone and one or more pharmaceutically acceptable carriers, diluents and excipients, which, for the extensive reasoning provided *supra*, and those reasons already made of record in previous Office Actions, is met by the teachings of Burchardt et al., absent factual evidence to the contrary. Note also that, although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

For these reasons, and those previously made of record at p.4-8 of the Office Action dated October 21, 2008, rejection of claims 40-42, 44-46 and 48-50 is proper.

Conclusion

Rejection of claims 40-42, 44-46 and 48-50 is proper.

Claims 43, 47 and 51 are objected to for depending from a rejected base claim.

No claims of the present application are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the

mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LESLIE A. ROYDS whose telephone number is (571)272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

June 29, 2009

/Ardin Marschel/
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